FORM PTO-1390 (REV. 11-2000) — U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U.S. APPLICATION NO. (If known, see 37 CFR 1.5)
0020-4883P	09/890552 NEW

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/JP99/07008	December 14, 1999	NONE

TITLE OF INVENTION

DRUG FOR ALLEVIATING MIGRAINE

APPLICANT(S) FOR DO/EO/US

YOKOYAMA, Hideakira; HAMAMOTO, Hidetoshi

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39 (1).
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau. WO 01/43736
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☒ is transmitted herewith.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4)
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). **(Original)**
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 20. below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.International Search Report (PCT/ISA/210) and PTO-1449
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821-1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☒ Other items or information:
    1.) ZERO (0) sheet Formal Drawings

JC05 Rec'd PCT/PTO 0 2 AUG 2001

U.S. APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/890552 NEW	PCT/JP99/07008	0020-4883P

21. ☒ The following fees are submitted:

	CALCULATIONS	PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO. **$1,000.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO. **$710.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4). **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 860.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 0	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	13 - 20 =	0	X **$18.00**	$ 0	
Independent Claims	3 - 3 =	0	X **$80.00**	$ 0	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)		No	+ **$270.00**	$ 0	
			TOTAL OF ABOVE CALCULATIONS =	$ 860.00	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				$ 0	
			SUBTOTAL =	$ 860.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐20 ☐30 months from the earliest claimed priority date (37 CFR 1.492(f)).			+	$ 0	
			TOTAL NATIONAL FEE =	$ 860.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property			+	$ 40.00	
			TOTAL FEES ENCLOSED =	$ 900.00	
			Amount to be: refunded	$	
			charged	$	

☒ A check in the amount of $ **900.00** to cover the above fees is enclosed.

☐ Please charge my Deposit Account. No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-2448.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

Send all correspondence to:

Birch, Stewart, Kolasch & Birch, LLP or Customer No. 2292
P.O. Box 747
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Date: August 2, 2001

By _____
Gerald M. Murphy, Jr., #28,977

PATENT
0020-4883P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	YOKOYAMA, Hideakira et al	Conf.:	
Int'l. Appl. No.:	PCT/JP99/07008		
Appl. No.:	NEW	Group:	
Filed:	August 2, 2001	Examiner:	
For:	DRUG FOR ALLEVIATING MIGRAINE		

PRELIMINARY AMENDMENT

BOX PATENT APPLICATION
Assistant Commissioner for Patents
Washington, DC 20231

August 2, 2001

Sir:

The following Preliminary Amendments and Remarks are respectfully submitted in connection with the above-identified application.

AMENDMENTS

IN THE SPECIFICATION:

Please amend the specification as follows:

Before line 1, insert --This application is the national phase under 35 U.S.C. § 371 of PCT International Application No. PCT/JP99/07008 which has an International filing date of December 14, 1999, which designated the United States of America.

IN THE CLAIMS:

Please amend the claims as follows:

3. (Amended) The drug claimed in claim 1, wherein the external migraine-alleviating drug is a patch.

REMARKS

The specification has been amended to provide a cross reference to the previously filed International Application.

The claims have been amended to place the application into better form prior to examination.

Entry of the present Amendment and favorable action on the merits are respectfully requested.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

BY _____
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GMM/tf
0020-4883P

(Rev. 02/12/01)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims have been amended as follows:

3. (Amended) The drug claimed in claim 1, wherein the external migraine-alleviating drug [for a local application] is a patch[and l-menthol and an essential oil are incorporated in its base].

DESCRIPTION

DRUG FOR ALLEVIATING MIGRAINE

TECHNICAL FIELD

The present invention relates to an external drug for dermal application, such as ointments or patches, in more detail, patches comprising in mixing l-menthol and an essential oil into a base containing a hydrophilic high-molecular weight compound, a polyhydric alcohol and water, which have a migraine-alleviating effect.

BACKGROUND ART

The cause of migraine is not clear, but it is considered that blood stream increases by expansion of head or cervix blood vessel due to hormone unbalance, and then muscle around that contracts. As a result migraine is caused.

For the treatment of migraine, analgesics for an internal application which contain ergotamine tartrate, dimethothiazine mesylate, caffeine, etc., as an active ingredient are used. However, such a drug is often administered for long term and therefore, there is a possibility to induce side effects such as, anaphylaxis, insomnia, or gastrointestinal disorder.

Accordingly, various preparations for dermal

applications for treating migraine have been worked out.

For example, in Japanese Patent Publication B 6-67835, a composition that methysergide, anti-serotonin is dispersed in a hydrophilic polymer for systemic dermal application to prevent migraine is disclosed. Furthermore, in Japanese Patent Publication A Tokuhyo Hei 8-509749, a dermally therapeutic system containing sumatriptan useful for migraine, cluster headache, etc., is disclosed.

However, these preparations for dermal application have a possibility to induce side effects, skin irritation, etc., by administering them for long term and therefore, these preparations are not favorable.

In addition, it is known that essential oils alleviate headache in using as an aromatherapy, but they have a demerit being lack in simplicity on their use.

The present inventors have extensively studied in order to obviate above mentioned demerits, and as a result, have unexpectedly found that migraine can be alleviated by dermally administering to human a drug containing l-menthol and an essential oil as active ingredients. Thus, the present invention has been completed.

DISCLOSURE OF INVENTION

The drug having a migraine-alleviating effect of the present invention is a drug for a locally dermal

application containing l-menthol and an essential oil as active ingredients. Its preferable preparations are ointments or patches, especially patches comprising in mixing l-menthol and an essential oil as active ingredients into a base containing hydrophilic high-molecular weight compound, a polyhydric alcohol and water.

The drug of the present invention is prepared by mixing l-menthol and an essential oil with a known base and if necessary, surfactants, preservatives, etc. to make into ointments or patches by the conventional method.

The amount of l-menthol admixed is for example, 0.01% - 1% by weight per total weight of base, preferably 0.05% - 0.5% by weight per total weight of base.

The essential oils used in the present invention are lavender oil, juniper oil, peppermint oil, rose oil, rosemary oil, etc. or a mixture thereof. The amount of these oils is 0.001% - 1% by weight per total weight of base, preferably 0.005 - 0.5% by weight per total weight of base.

In ointments, known bases such as white vaseline, yellow vaseline, lanolin, purified beeswax, cetanol, stearyl alcohol, hydrogenated oil, hydrocarbon gel, polyethylene glycol, etc. are used. To these bases, l-menthol and an essential oil and if necessary, surfactants, preservatives, purified water, etc. are mixed to prepare

ointments.

The especially preferable preparations of the present invention are patch-preparations which are prepared by mixing l-menthol and an essential oil as active ingredients into the base containing a hydrophilic high-molecular weight compound, polyhydric alcohol and water.

The patches of the present invention are in more detail explained as follows.

The hydrophilic high-molecular weight compounds used in the patches include, for example, gelatin, polyacrylic acid and its salt, polyvinyl alcohol, polyvinylpyrrolidone, carboxyvinyl polymer, sodium carboxymethyl cellulose, hydroxypropyl cellulose, methyl cellulose, ethyl cellulose, methyl vinyl ether·maleic acid anhydride copolymer, sodium alginate, poly ethylene oxide, acacia gum, xanthan gum, tragacanth gum, etc. These may be used in a mixture thereof.

The amount of the hydrophilic high-molecular weight compound is not limited, but when its amount is less than 2% by weight per total weight of base, the base is lack in viscosity not to become paste. On the other hand, when its amount is more than 20% by weight per total weight of base, it may occur that viscosity of the base becomes too high to smoothly prepare the preparation. Therefore, the amount of the hydrophilic high-molecular weight compound is 2-20% by

weight per total weight of base, preferably 5-15% by weight per total weight of base.

The polyhydric alcohols include glycerin, sorbitol, propylene glycol, polyethylene glycol, 1,3-butylene glycol, ethylene glycol, etc. These may be used in a mixture thereof.

The amount of the polyhydric alcohol is 8 - 60% by weight per total weight of base, preferably 10 - 50% by weight per total weight of base.

When its amount is less than 8% by weight per total weight of base, humidity-keeping effect becomes poor and water become volatile in short times. On the other hand, when its amount is more than 60% by weight per total weight of base, it is difficult to mix with other substances and to use the polyhydric alcohol so much is not desirable.

The amount of water is 20 - 80% by weight per total weight of base, preferably 25 - 70% by weight per total weight of base.

When its amount is less than 20% by weight per total weight of base, dissolution of the hydrophilic high-molecular weight compound is not satisfactory and it is impossible to homogeneously extend the base. On the other hand, when its amount is more than 80% by weight per total weight of base, it may occur that the base becomes too soft to spread out. Therefore, it is not desirable to use water

so much.

The amount of l-menthol is 0.01-1% by weight per total weight of base, preferably 0.05-0.5% by weight per total weight of base as mentioned above. The amount of the essential oil is 0.001-1% by weight per total weight of base, preferably 0.005-0.5% by weight per total weight of base as mentioned above.

In addition to the above mentioned base, following additives which are usually used in patches can be mixed in the usual amount: excipients (kaolin, bentonite, titanium oxide, etc.), surfactants (glycerin fatty acid ester, polyoxyethylene castor oil, polyoxyethylene hydrogenated castor oil, sorbitan fatty acid ester, polysolbate 80, polysolbate 60, solbitan sesquioleate), crosslinking agents (multivalent metal such as aluminum hydroxide, aluminum glycinate, dihydroxyaluminum aminoacetate, synthetic hydrotalcite, etc.), coloring agents (new coccin, tartrazine, brilliant blue FCF), and preservatives (p-hydroxybenzoic acid ester, sorbic acid salt, isopropyl methyl phenol, hinokitiol, phenoxyethanol, etc.)

The base is prepared by mixing each ingredient in accordance with the conventional method. For example, a part of a hydrophilic high-molecular weight compound and a polyhydric alcohol are dissolved in water, and if desired, other additives are mixed, and then l-menthol and an

essential oil are added to the mixture to be kneaded. Then, residual of the hydrophilic high-molecular weight compound and other additives are mixed thereto to prepare the base.

The base thus prepared is spread on an appropriate support and a releasing paper is put on the base in order to protect the base. The base cut in a fixed size to prepare desired patches.

The amount of the base in patches is 200-5000g/m^2, preferably 500-2000g/m^2.

The support is one such as non-woven fabrics, fabrics, knits, etc., used in usual patches. Its material is an synthetic fiber such as nylon, rayon, polyester, polypropylene, etc. or a natural fiber such as cotton. As the releasing paper, plastic film such as polyethylene film, etc. and others used in usual patches are used.

Shapes of the patches may be ellipse, rectangle, triangle, boomerang type, facemask type, etc.

The patches of the present invention are preferably applied to on forehead, nape of the neck, temple, a half of face and/or full face, and by doing the patch thereto, migraine-alleviating effect effectively appears.

BEST MODE FOR CARRYING OUT THE INVENTION

The present invention and its effect are illustratively explained by working examples and tests, but

the invention should not be limited by these examples.

Examples 1-6

Using ingredients shown in Tables 1 and 2, patches (Examples 1-6) were prepared by the conventional method. Namely, a part of the hydrophilic high-molecular weight compound and the polyhydric alcohol were dissolved in purified water, and if necessary, other ingredients were added thereto. The mixture was fully kneaded. Then, l-menthol and the essential oil were added to the mixture and further, the residue of the hydrophilic high-molecular weight compound and other ingredients were added to. Finally, the residue of the purified water was added to the mixture. The mixture was homogeneously kneaded to prepare a base.

The base prepared was spread on the support (1000g/m^2) and a releasing paper or plastic film was put on it. The base was cut into a fixed size to prepare patches.

The bases prepared above, as such may be used as ointments.

Table 1.

Ingredients	Percent by Weight		
	Example 1	Example 2	Example 3
Polyacrylic acid	1.0	2.5	1.25
Sodium polyacrylate	5.0	6.0	6.0
Sodium carboxy methylcellulose	5.0	4.0	5.5
Gelatin	0.4	-	0.2
Polyvinyl alcohol	0.2	-	-
Tartaric acid	0.2	0.15	0.25
Disodium edetate	0.1	0.08	0.07
Glycerin	22.0	15.0	18.0
70% Sorbitol solution	-	15.0	-
Aluminum hydroxide	0.3	-	-
Synthetic hydrotalcite	-	0.2	-
Dihyroxyaluminum acetate	-	-	0.08
Polysolbate 80	0.1	0.1	0.1
Caster oil	0.5	0.5	0.5
Methylparaben	0.1	0.1	0.1
l-Menthol	0.3	0.15	0.1
Peppermint oil	0.2	-	-
Rose oil	-	0.1	-
Lavender oil	-	-	0.01
Purified water	Residue	Residue	Residue
	100	100	100

Table 2.

Ingredients	Percent by Weight		
	Example 4	Example 5	Example 6
Polyacryric acid	1.5	2.0	1.25
Sodium polyacrylate	5.0	5.5	6.0
Sodium carboxy methylcellulose	5.0	4.0	5.5
Gelatin	–	–	–
Polyvinyl alcohol	0.2	–	–
Tartaric acid	0.2	0.15	0.3
Disodium edetate	0.1	0.08	0.07
Glycerin	20.0	15.0	20.0
70% Sorbitol solution	10.0	15.0	–
Aluminum hydroxide	0.3	–	–
Synthetic hydrotalcite	0.15	–	–
Dihydroxyaluminum acetate	–	0.1	0.1
Polysolbate 80	0.1	0.1	0.1
Caster oil	0.5	0.5	0.5
Methylparaben	0.1	0.1	0.1
l-Menthol	0.8	0.25	0.05
Peppermint oil	0.2	0.4	–
Rose oil	–	0.4	0.05
Lavender oil	0.05	–	0.1
Purified water	Residue	Residue	Residue
	100	100	100

Comparative example 1

The patch was prepared by the same method as Example 1 using the same ingredients as Example 1 provided that the

same amount of water as l-menthol was used instead of l-menthol (Only an essential oil is used as an active ingredient).

Comparative example 2

The patch was prepared by the same method as Example 1 using the same ingredients as Example 1 provided that the same amount of water as an essential oil was used instead of the essential oil (Only l-menthol is used as an active ingredient).

Comparative example 3

The patch was prepared by the same method as Example 1 using the same ingredients as Example 1 provided that the same amount of water was used instead of the essential oil and l-menthol (Any active ingredient was not used).

Next, each two patches (5x7cm) of Examples 1, 3, 5 and Comparative examples 1-3 were put on each volunteer. The following items were sensitively evaluated.

Test 1

On their foreheads of ten volunteers suffering from migraine were put each patch of Examples 1, 3, 5 and Comparative examples 1-3, and migraine-alleviating effect

was evaluated by sensory test under following evaluation-standards.

Evaluation-standard on effects

Point 1: no effect

Point 2: weak effect

Point 3: effective

Point 4: clearly effective

Point 5: strongly effective

Efficacy (point) was indicated by the average of volunteer's evaluations. The duration of the effect was indicated by the average of volunteer's reported times.

The result was shown in the following Table 3.

Table 3

	Efficacy(point)	Duration of effect(hour)
Example 1	4.2	7.3
Example 3	4.3	7.9
Example 5	3.9	6.5
Comparative example 1	2.5	3.2
Comparative example 2	2.8	2.8
Comparative example 3	1.3	2.1

As is clear from the result of Table 3, patches of Examples 1, 3 and 5 were superior in efficacy (point) to patches of Comparative examples 1-3, and therefore, it is

recognized that patches of Examples 1, 3 and 5 are excellent in migraine-alleviating effect and that its effect lasts for long hours.

Test 2

On various regions of ten volunteers suffering from migraine were put each patch of Examples 1, 3, 5 and Comparative example 3, and migraine-alleviating effect depending on the region was evaluated by sensory test under following evaluation-standards.

Evaluation standard:

+ : Positive alleviating efficacy

± : Weak alleviating efficacy

- : No alleviating efficacy

The result is shown in Table 4.

Table 4.

Application region	Alleviating efficacy			
	Example 1	Example 3	Example 5	Comparative example 3
Forehead	+	+	+	±
Nape of neck	+	+	+	-
Temple	+	+	+	±
Shoulder	±	±	±	-
Back	-	-	-	-
Breast	-	-	-	-

As is clear from the result of Table 4, when applying the preparations of the present invention, that is preparations of Examples 1, 3 and 5 to face, nape of the neck and temple, the preparations were recognized being superior in migraine-alleviating efficacy. On the other hand, a patch of Comparative example 3 hardly showed migraine-alleviating efficacy in any region.

INDUSTRIAL APPLICABILITY

The preparation of the present invention is excellent in migraine-alleviating efficacy, and even when using for long terms, there is hardly a possibility to induce side effects and the preparation of the present invention is very convenient and useful.

CLAIMS

1. An external migraine-alleviating drug for a local application, consisting of l-menthol and an essential oil as active ingredients.

2. The drug claimed in claim 1, wherein the external migraine-alleviating drug for a local application is an ointment.

3. The drug claimed in claim 1, wherein the external migraine-alleviating drug for a local application is a patch, and l-menthol and an essential oil are incorporated in its base.

4. The drug claimed in claim 1, wherein the external migraine-alleviating drug for a local application is in a patch prepared by mixing l-menthol and an essential oil as active ingredients into a base containing a hydrophilic high-molecular weight compound, a polyhydric alcohol and water.

5. The patch claimed in claim 4, wherein the essential oil is at least one essential oil selected from the group consisting of lavender oil, juniper oil, peppermint oil, rose oil and rosemary oil.

6. The patch claimed in claim 4, wherein the amounts of l-menthol and the essential oil are 0.01-1% by weight per total weight of base and 0.001-1% by weight per total weight of base, respectively.

7. The patch claimed in claim 4, wherein the amounts of a hydrophilic high-molecular weight compound, a polyhydric alcohol and water are 2-20% by weight per total weight of base, 8-60% by weight per total weight of base and 20-80% by weight per total weight of base, respectively.

8. The patch claimed in claim 4, wherein shape of the patch is rectangle, ellipse, triangle, boomerang type or facemask type.

9. Use of only l-menthol and an essential oil as active ingredients for preparing an external migraine-alleviating drug for a local application.

10. The use claimed in claim 9, wherein the external migraine-alleviating drug for a local application preparation is a patch.

11. A therapeutic method for alleviating migraine by dermally administrating a drug containing l-menthol and an essential oil in an effective amount to the patient.

12. The method claimed in claim 11, wherein the drug is a patch.

13. The method claimed in claim 11, wherein an application region of the drug is face, forehead, nape of the neck or temple.

ABSTRACT

This invention relates to external drugs for dermal application which have a migraine-alleviating effect, in more detail ointments and patches comprising in mixing l-menthol and an essential oil into a base containing a hydrophilic high-molecular weight compound, a polyhydric alcohol and water.

Attorney Docket No.

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0020-4883P

PLEASE NOTE: YOU MUST COMPLETE THE FOLLOWING

COMBINED DECLARATION AND POWER OF ATTORNEY FOR PATENT AND DESIGN APPLICATIONS

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated next to my name; that I verily believe that I am the original, first and sole inventor (if only one inventor is named below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Insert Title: DRUG FOR ALLEVIATING MIGRAINE

Fill in Appropriate Information - For Use Without Specification Attached:

the specification of which is attached hereto. If not attached hereto,
the specification was filed on _____ as
United States Application Number _____;
and amended on _____ (if applicable) and/or
the specification was filed on December 14, 1999 as PCT
International Application Number PCT/JP99/07008; and was
amended under PCT Article 19 on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I do not know and do not believe the same was ever known or used in the United States of America before my or our invention thereof, or patented or described in any printed publication in any country before my or our invention thereof or more than one year prior to this application, that the same was not in public use or on sale in the United States of America more than one year prior to this application, that the invention has not been patented or made the subject of an inventor's certificate issued before the date of this application in any country foreign to the United States of America on an application filed by me or my legal representative or assigns more than twelve months (six months for designs) prior to this application, and that no application for patent or inventor's certificate on this invention has been filed in any country foreign to the United States of America prior to this application by me or my legal representatives or assigns, except as follows.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Insert Priority Information: (if appropriate)

Prior Foreign Application(s)			Priority Claimed	
(Number)	(Country)	(Month/Day/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Month/Day/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Month/Day/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Month/Day/Year Filed)	☐ Yes	☐ No

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional applications(s) listed below.

Insert Provisional Application(s): (if any)

(Application Number)	(Filing Date)
(Application Number)	(Filing Date)

All Foreign Applications, if any, for any Patent or Inventor's Certificate Filed More than 12 Months (6 Months for Designs) Prior to the Filing Date of This Application:

Insert Requested Information: (if appropriate)

Country	Application Number	Date of Filing (Month/Day/Year)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States and/or PCT application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States and/or PCT application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Insert Prior U.S. Application(s): (if any)

(Application Number)	(Filing Date)	(Status - patented, pending, abandoned)
(Application Number)	(Filing Date)	(Status - patented, pending, abandoned)

Attorney Docket No.

I hereby appoint the following attorneys to prosecute this application and/or an international application based on this application and to transact all business in the Patent and Trademark Office connected therewith and in connection with the resulting patent based on instructions received from the entity who first sent the application papers to the attorneys identified below, unless the inventor(s) or assignee provides said attorneys with a written notice to the contrary:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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